CLAIMS

1. A method of increasing apoptosis in a cell, said method comprising administering to said cell an apoptosis inducing amount of an E4orf6 polypeptide or apoptotic fragment thereof.

2. The method of claim 1, wherein said apoptosis is p53-independent.

3. A method of increasing apoptosis in a mammal, said method comprising providing a transgene encoding an apoptotic E4orf6 polypeptide or an apoptotic fragment thereof to a cell of said mammal, said transgene being positioned for expression in said cell.

4. A method of increasing apoptosis in a cell, said method comprising administering a compound which increases E4orf6 mediated E4orf6 biological activity.

5. The method of claim 1 or 4, wherein said cell is in a mammal.

6. The method of claim 5, wherein said mammal is a human.

7. The method of claim 1, 3, or 4, wherein said cell is in a mammal diagnosed as having a disease involving insufficient apoptosis.

8. The method of claim 7, wherein said disease is cancer.

9. The method of claim 4, wherein said compound is E4orf6 mRNA.

10. The method of claim 4, wherein said compound increases stability of E4orf6.

11. A method of increasing apoptosis in a cell, said method comprising administering to said cell an apoptosis inducing amount of an E4orf4 polypeptide or an apoptotic fragment thereof.

12. The method of claim 11, wherein said apoptosis is p53-independent.

13. A method of increasing apoptosis in a mammal, said method comprising providing a transgene encoding an apoptotic E4orf4 polypeptide or an apoptotic fragment thereof to a cell of said mammal, said transgene being positioned for expression in said cell.

14. A method of increasing apoptosis in a cell, said method comprising administering a compound which increases E4orf6 mediated E4orf6 biological activity.

15. The method of claim 11 or 14, wherein said cell is in a mammal.

16. The method of claim 15, wherein said mammal is a human.

17. The method of claim 11, 13, or 14, wherein said cell is in a mammal diagnosed as having a disease involving insufficient apoptosis.

18. The method of claim 17, wherein said disease is cancer.

19. The method of claim 14, wherein said compound is E4orf4 mRNA.

20. The method of claim 14, wherein said compound increases the stability of E4orf4.

21. A method of increasing apoptosis in a cell, said method comprising administering to said cell an apoptosis inducing amount of a composition comprising and E4orf6 polypeptide or an apoptotic fragment thereof and an E4orf4 polypeptide or an apoptotic fragment thereof.

22. The method of claim 21, wherein said apoptosis is p53-independent.

23. A method of increasing apoptosis in a mammal, said method comprising providing a first transgene encoding an E4orf6 polypeptide or an apoptotic fragment thereof and a second transgene encoding an E4orf4 polypeptide or an apoptotic fragment thereof to a cell of said mammal, said first transgene and said second transgene being positioned for expression in said cell.

24. A method of increasing apoptosis in a cell, said method comprising administering a composition comprising a first compound which increases E4orf6 mediated E4orf6 biological activity and a second compound which increases E4orf6 mediated E4orf4 biological activity.

25. The method of claim 21 or 24, wherein said cell is in a mammal.

26. The method of claim 25, wherein said mammal is a human.

27. The method of claim 21, 23, or 24, wherein said cell is in a mammal diagnosed as having cancer.

28. The method of claim 23, wherein said first transgene and said second transgene encodes E4orf4 are linked to a constitutive promoter.

29. The method of claim 24, wherein said first compound is E4orf6 mRNA and said second compound is E4orf4 mRNA

30. The method of claim 24, wherein said first compound and said second compound increase stability of E4orf6 and E4orf4.

31. A pharmaceutical composition comprising substantially pure nucleic acid encoding an E4orf6 polypeptide and a pharmaceutically acceptable carrier.

32. The composition of claim 31, wherein said nucleic acid encodes E4orf6 having a conservative amino acid substitution relative to the E4orf6 sequence of Fig. 15 (SEQ ID NO.: 2).

33. A pharmaceutical composition comprising substantially pure nucleic acid encoding an apoptotic fragment of E4orf6.

34. The composition of claim 31 or 33, wherein said nucleic acid is in a viral vector.

35. A pharmaceutical composition comprising nucleic acid having the sequence of Fig. 15 (SEQ ID NO.: 1), or degenerate variants thereof, and encoding the amino acid sequence of Fig. 15 (SEQ ID NO.: 2).

36. A pharmaceutical composition comprising nucleic acid having about 50% or greater nucleotide sequence identity to the DNA sequence of Fig. 15 (SEQ ID NO.: 1), said nucleic acid encoding a polypeptide with E4orf6 biological activity.

37. The composition of claim 36, wherein said nucleotide sequence identity is 75% or greater to the DNA sequence of Fig. 15 (SEQ ID NO.: 1).

38. A pharmaceutical composition comprising a DNA sequence substantially identical to the DNA sequence shown in Fig. 15 (SEQ ID NO.: 1).

39. The composition of claim 31 or 33, wherein said nucleic acid is operably linked to regulatory sequences for expression of said polypeptide and wherein said regulatory sequences comprise a promoter.

40. The composition of claim 39, wherein said promoter is a constitutive promoter, is inducible by one or more external agents, or is cell-type specific.

41. A pharmaceutical composition comprising substantially pure E4orf6 polypeptide, or an apoptotic fragment thereof.

42. The composition of claim 41, wherein said polypeptide comprises an amino acid sequence substantially identical to an amino acid sequence shown in Fig.15 (SEQ ID NO.: 2).

43. The composition of claim 41, wherein said polypeptide has a conservative amino acid substitution relative to the E4orf6 sequence of Fig. 15 (SEQ ID NO.: 2)

44. A pharmaceutical composition comprising a substantially pure polypeptide fragment of E4orf6.

45. A pharmaceutical composition comprising substantially pure nucleic acid encoding an E4orf4 polypeptide and a pharmaceutically acceptable carrier.

46. The composition of claim 45, wherein said nucleic acid encodes E4orf4 having a conservative amino acid substitution relative to the E4orf4 sequence of Fig. 16 (SEQ ID NO.: 4).

47. A pharmaceutical composition comprising substantially pure nucleic acid encoding an apoptotic fragment of E4orf4.

48. The composition of claim 45 or 47, wherein said nucleic acid is in a viral vector.

49. A pharmaceutical composition comprising nucleic acid having the sequence of Fig. 16 (SEQ ID NO.: 3), or degenerate variants thereof, and encoding the amino acid sequence of Fig. 16 (SEQ ID NO.: 4).

50. A pharmaceutical composition comprising nucleic acid having about 50% or greater nucleotide sequence identity to the DNA sequence of Fig. 16 (SEQ ID NO.: 3), said nucleic acid encoding a polypeptide with E4orf4 biological activity.

51. The composition of claim 50, wherein said nucleotide sequence identity is 75% or greater to the DNA sequence of Fig. 16 (SEQ ID NO.: 3).

52. A pharmaceutical composition comprising a DNA sequence substantially identical to the DNA sequence shown in Fig. 16 (SEQ ID NO.: 3).

53. The composition of claim 45 or 47, wherein said nucleic acid is operably linked to regulatory sequences for expression of said polypeptide and wherein said regulatory sequences comprise a promoter.

54. The composition of claim 53, wherein said promoter is a constitutive promoter, is inducible by one or more external agents, or is cell-type specific.

55. A pharmaceutical composition comprising substantially pure mammalian E4orf4 polypeptide, or an apoptotic fragment thereof

56. The composition of claim 55, said polypeptide comprising an amino acid sequence substantially identical to an amino acid sequence shown in Fig. 16 (SEQ ID NO.: 4).

57. The composition of claim 55, wherein said polypeptide has a conservative amino acid substitution relative to the E4orf4 sequence of Fig. 16 (SEQ ID NO.: 4).

58. A pharmaceutical composition comprising a substantially pure polypeptide fragment of E4orf4.

59. A method for identifying a compound as an E4orf6 or E4orf4 analog, said method comprising the steps of:

a) providing a cell expressing the adenovirus E1A-289R protein, said cell not expressing any E4 proteins;

b) contacting said cell with a candidate compound; and

c) determining viability of said cell, wherein apoptotic death of said cell indicates a compound that is an E4orf6 analog.

60. A method for identifying a compound as an E4orf4 analog, said method comprising the steps of:

a) providing a cell expressing the adenovirus E1A-289R protein, said cell not expressing any E4 proteins;

b) contacting said cell with a candidate compound; and

c) determining viability of said cell, wherein apoptotic death of said cell indicates a compound that is an E4orf4 analog.

61. The method of claim 59, wherein said cell is selected from the group consisting of: 1A.A3, 1A.A6, and 1A.A12 cells.

62. The method of claim 59, wherein said viability is measured with Trypan Blue™.

63. The method of claim 59, wherein said viability is measured with a DNA fragmentation assay.

64. The method of claim 59, wherein said viability is measured with Annexin V binding.

65. The method of claim 59, wherein said viability is measured with Propidium Iodide

66. The method of claim 59, wherein said viability is measured utilizing a combination of two or more of the following: Trypan Blue™, DNA fragmentation, Annexin V binding, and Propidium Iodide.

67. The method of claim 59, wherein said cell is a cell is infected with a mutant adenovirus, said mutant adenovirus incapable of expressing any E4 proteins.

68. A method for identifying a compound as an E4orf4 analog, said method comprising the steps of:

a) providing a cell expressing protein phosphatase 2A;

b) contacting said cell with a candidate compound; and

c) measuring activity of said protein phosphatase 2A in said cell, an increase in said activity relative to a cell not contacted with said candidate compound indicating a compound that is an E4orf4 analog.

69. A pharmaceutical agent for induction of apoptosis for the treatment of human diseases which involve inappropriate cell survival, which comprises E4orf6, an analog or a biologically active fragment thereof.

70. A pharmaceutical composition for the treatment of human diseases which involve inappropriate cell survival, which comprises a therapeutical amount of E4orf6, an analog or a biologically active fragment thereof in association with a pharmaceutical carrier.

71. A pharmaceutical composition for the treatment of human diseases which involve inappropriate cell survival, which comprises a therapeutic amount of a compound which induces apoptosis or other cytotoxic effects analogous to E4orf6 biological activity in association with a pharmaceutical carrier.

72. A pharmaceutical agent for induction of apoptosis for the treatment of human diseases which involve inappropriate cell survival, which comprises E4orf4, an analog or a biologically active fragment thereof.

73. A pharmaceutical composition for the treatment of human diseases which involve inappropriate cell survival, which comprises a therapeutic amount of E4orf4, an analog or a biologically active fragment thereof in association with a pharmaceutical carrier.

74. A pharmaceutical composition for the treatment of human diseases which involve inappropriate cell survival, which comprises a therapeutic amount of a compound which induces protein phosphatase 2a in association with a pharmaceutical carrier.

75. The composition of claim 74, wherein said compound is an agonist of E4orf4.

76. The composition of claim 74, wherein said compound mimics E4orf4 activity.

77. A pharmaceutical composition for the treatment of human diseases which involve inappropriate cell survival, which comprises a therapeutic amount of a compound which induces apoptosis or other cytotoxic effects analogous to E4orf4 biological activity in association with a pharmaceutical carrier.

78. A pharmaceutical agent for induction of apoptosis for the treatment of human diseases which involve inappropriate cell survival, which comprises E4orf6, an analog or a biologically active fragment thereof; and E4orf4, an analog or a biologically active fragment thereof.

79. A pharmaceutical composition for the treatment of human diseases which involve inappropriate cell survival, which comprises a therapeutical amount of E4orf6, an analog or a biologically active fragment thereof; and E4orf4, an analog or a biologically active fragment thereof in association with a pharmaceutical carrier.

80. A pharmaceutical composition for the treatment of human diseases which involve inappropriate cell survival, which comprises a therapeutic amount of a

compound which induces apoptosis or other cytotoxic effects analogous to biological activities of the E4 death proteins in association with a pharmaceutical carrier.